10-6-83

OCT 6 1983

Caswell No(s).: 215 D

To: Taylor/Rommens

Registration No(s).:

Pesticide Petition No(s).: 352-EUP-RRE

Chemical(s): DPX-Y6202, new chemical

accession numbers
250071
250072 004589
250073
250554

Requested Action(s): Experimental use permit "for use under Circa Fallow".

Recommendation: The EUP can be toxicologically supported provided that RCB concurs that this is a non-food-crop use.

Inert(s) cleared 180.1001: Aldicarb

% of ADI occupied: Existing: comments Resulting: on data

Resulting % increase in TMRC: requirements which will

Data considered in setting the ADI: be needed for registration

must be cleared

Attached (?): ADI printout: ~~YES~~/NO; TOX "one-liner": YES/NO; DER: YES/NO

Chiefs regulatory actions against registration:

RPAR status:

BEST AVAILABLE COPY

New Data: See reviews attached

Data gaps: The ingestion study requirements. Additional data will be required for registration

Comments: See attached comments on living fallow

9/24

Reviewer: R. Rommens 9-16-83 Date: OCT 6 1983

Section Head: William M Butler 9/26/83 Branch Chief: Clifford 10/6/83

TOXICOLOGY BRANCH
DATA REVIEW

Study Type: Acute Oral Toxicity in rats

Accession Number: 250071 (c 1)

MRID Number:

Sponsor: DuPont

Contracting Lab: Haskell Lab. report No. 136-83

Date: 4-11-83

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-,ethyl ester. EC formulation (10.5%) DPX-Y6202-7

Protocol:

Five males and 5 females were each given one oral dose, 5000 mg/kg.

Results:

"Clinical signs included: tremors, fasciculations, salivation, ataxia, stained face, stained and/or wet perineal area, diarrhea, alopecia, prostration, moribundity and weight loss. Death occurred in 1 male rat within 1 day after dosing."

"Gross pathology revealed large livers in 4/4 of surviving male and 4/5 female rats; and lungs which were moist, failed to collapse, and contained dull red mottling in a single male rat."

Conclusion:

LD50 males: > 5000 mg/hg Category IV
LD50 females: > 5000mg/kg

Core Classification:

Guideline.

TOXICOLOGY BRANCH DATA REVIEW

Study Type: Acute dermal toxicity in rabbits

Accession Number: 250071 (C 2)

MRID Number:

Sponsor: Du Pont

Contracting Lab: Hazleton Lab. Project No. 201-590

Date: 3-28-83

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-, ethyl ester. EC formulation (10.5%) DPX-Y6202-7.

Protocol:

Groups and dosages were as follows.

No. of Animals		Application Level
Males	Females	mg/kg
5	5	2000
5	5	5000

The test material was applied to clipped and abraded skin, covered with a non-absorbent binder and allowed to remain in contact for 24 hours. The excess was then wiped off.

Results:

The only death was that of one male of the 5000 mg/kg dosage level.

Clinical signs consisted of depression and anorexia in some but not all animals. A cyanotic appearance was seen in 2 males of the 5000 mg/kg groups. One of the two died. No visceral pathology was noted in either group.

Considerable skin damage was reported. In addition to edema and erythema, skin thickening, necrosis, sloughing, raw areas, eschar, and (in the 5000 mg/kg group) black discoloration were seen.

Conclusion:

Acute dermal toxicity category: III

Categorization for skin damage has been evaluated from a dermal irritation test.

Core Classification: Minimum for Category III

004589

DL-7

TOXICOLOGY BRANCH DATA REVIEW

Study Type: Acute inhalation toxicity in rats

Accession Number: 250071 (C 3)

MRID Number:

Sponsor: Du Pont

Contracting Lab: Haskell Lab. Report No. 156-83

Date: 4-25-83

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-, ethyl ester. EC formulation (10.5%) DPX-Y6202-7.

Groups of rats were exposed to atmospheres containing DPX-Y6202-7 or the solvent for single, 4-hour periods. Only noses were exposed. Also a control group was exposed to air only. Gross pathology was performed on rats dying during exposure (up to 3 per sex per group) and on 3 rats per sex per group which survived 14 days post exposure.

Group sizes and dosages are shown in table below with results.

Results:

DPX-Y6202-7

Concentration (mg/L)			Fractional Mortality (#Deaths/#Exposed)	
Mean	S.D.	Range	Males	Females
5.3+	0.38	4.9 - 5.8	0/10	0/10
11*	0.93	9.4 - 12	1/10	1/10
12+	1.0	11 - 14	0/10	1/10
23*	1.8	20 - 25	7/10	8/10
36*	2.3	32 - 38	10/10	10/10

Solvent for INY-6202-7:

Concentration (mg/L)			Fractional Mortality (#Deaths/#Exposed)	
Mean	S.D.	Range	Males	Females
11+	0.99	9.1 - 12	0/10	0/10
21+	1.0	15 - 33	0/10	0/10

+ Gas chromatographic analytical method
* Gravimetric analytical method

Gravimetric and chromatographic analytical methods agreed within 20%. The method on which reported concentration is based is annotated below:

All deaths occurred during exposure except of one rat at 36 mg/l.

"Clinical signs for rats exposed to DPX-Y6202-7 include milky nasal discharge, clear oral discharge, labored breathing, gasping, no response to sound, staggering, lethargic or no movement, and impaired righting reflex during exposures. During the recovery period, rats exhibited dose-dependent slight to severe weight loss lasting 1-2 days post-exposure.

Clinical signs for rats exposed to the solvent for DPX-Y6202-7 alone include clear nasal and oral discharge, no response to sound, slow shallow breathing, decreased muscle tone and no movement during exposures. During the recovery period, rats exhibited dose-dependent slight to severe weight loss lasting 1 day post exposure.

Pathological examination revealed a slight to mild increase in the number of mitotic figures in the liver in all exposed rats (DPX-Y6202-7 and the solvent alone). No dose-response in the incidence of the lesion was observed."

"Rats exposed to 23 and 36 mg/L which died during exposures exhibited distension of hepatic sinusoids, pulmonary congestion and pulmonary interstitial edema. These changes are associated with circulatory collapse," and may not be a direct result of compound toxicity.

Conclusions:

LC50 for males: 20 (17-25) mg/l Category III
LC50 for females: 18 (15-23) mg/l

Some toxic effects are apparently caused by solvent.

Core Classification

Guideline

004589

TOXICOLOGY BRANCH
DATA REVIEW

01-5

Study Type: Eye irritation in rabbits

Accession Number: 250071 (c4)

MRID Number:

Sponsor: DuPont

Contracting Lab: Haskell Lab report no. HLO 117-83

Date: April 11, 1983

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-, ethyl ester. E.C. formulation (10.5%) DPX-Y6202-7.

Protocol:

EPA's proposed guidelines of 8-22-78 were followed.

Results:

The test material "produced slight to severe corneal opacity which was irreversible in three unwashed and one washed eye. Iritis occurred in all unwashed eyes and none of the washed eyes. Mild to severe conjunctival irritation occurred in all animals and mild to moderate irritation persisted throughout the study in some animals."

Conclusion:

Severe corneal opacity. Category I

Core classification:

Guideline

DCR-10663:W.T.Edwards:Tox-32:557-1511:CM#2:Rm824:efs:8/2/83

0L-4

TOXICOLOGY BRANCH DATA REVIEW

004589

Study Type: Primary dermal irritation in rabbits

Accession Number: 250071 (C 5)

MRID Number:

Sponsor: Du Pont

Contracting Lab: Haskell Lab. report no. HLO 130-83

Date: 4-14-83

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-, ethyl ester. EC formulation (10.5%) DPX-Y6202-7.

Protocol:

Six male rabbits were used. After clipping dorsal areas, 0.5 ml portions were applied to abraded and to intact skin of each animal. Material was covered with gauze and rubber damming. Material was wiped off after 24 hours. Dermal responses were observed after hours 24, 48, and 72 and after days 4, 7, and 14 from application. No necropsy was performed.

Results:

At 72 hours, in addition to erythema and edema, which reportedly resulted in a Draize score of 2.59, thickening of skins were seen in all animals. Necrosis and/or sloughing later also developed in the other animals.

The following table shows the occurrence of effects other than erythema and edema.

Animal Number	Exposure Site	Other Dermal Effects					
		24 Hours	48 Hours	72 Hours	Day 4	Day 7	Day 14
E32588	A/1	-	T	NT	N	NL	S
	A/2	-	N	NT	N	SL	-
	1/1	-	T	NT	N	SL	-
	1/2	-	T	T	N	N	S
E32589	A/1	-	T	T	T	SL	-
	A/2	-	T	T	T	N	-
	1/1	-	T	T	T	SL	-
	1/2	-	T	T	T	SL	-

Animal Number	Exposure Site	Other Dermal Effects					
		24 Hours	48 Hours	72 Hours	Day 4	Day 7	Day 14
E32590	A/1	-	T	T	N	N	S
	A/2	-	T	T	N	N	-
	1/1	-	T	T	N	N	-
	1/2	-	T	T	N	N	-
E32591	A/1	-	T	T	T	N	S
	A/2	-	T	T	T	N	-
	1/1	-	T	T	T	TS	S
	1/2	-	T	T	T	N	S
E32592	A/1	-	T	T	T	N	-
	A/2	-	T	NT	NT	N	S
	1/1	-	T	T	N	NL	-
	1/2	-	T	NT	NT	N	-
E32593	A/1	-	T	T	N	NF	S
	A/2	-	T	T	T	NF	-
	1/1	-	T	T	T	TF	S
	1/2	-	T	T	N	NF	S

A = Abraded
I = Intact
T = Thickening
B = Blanching
F = Fissuring
N = Necrosis
S = Epidermal Scaling
L = Sloughing
- = No Effect

Conclusions:

Primary dermal irritation, Category I is appropriate for this product.

Core classification: Guideline

004589

TOXICOLOGY BRANCH
DATA REVIEW

Study Type: Unscheduled DNA Synthesis in rat hepatocytes in vitro.

Accession Number: 250071 (C6)

MRID Number:

Sponsor: DuPont

Contracting Lab: Haskell Laboratory Report No. 140-83

Date: 4-15-83

Test Material: 2-4[4-6-chloroquinoxalin-2-yloxy)-phenoxy] ethyl ester, DPX-Y6202-6, technical.

Protocol:

Rat hepatocytes were used to perform two trials in an unscheduled DNA synthesis study. Concentrations ranged from 1 x 10^{-5}mM to 6.0 mM. The higher limit was the limit of solubility in solvent, acetone.

Results:

No increase in net grain count over solvent at any concentration. Positive control, DMBA gave positive results.

Conclusion

Negative

Evaluation:

Acceptable

TOXICOLOGY BRANCH
DATA REVIEW

Study Type: Micronucleus Test in CD-1 mice.

Accession Number: 250071(C7)

MRID Number:

Sponsor: Du Pont

Contracting Lab: Nissan chemical Industries, Ltd.

Date: 12-1-81

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-, ethyl ester (99.1%), DPX-Y6202, NC 302

Protocol:

Each of 8 animals per group were given orally 0, 300, 600, or 1200 mg/kg in corn oil (2 doses 24 hours apart) or as a positive control, 3 mg/kg Mitomycin-C, i.p. (one dose). Six hours after last dose, DPX-Y6202 treated animals were killed and frequency of polychromatic and normochromatic erythrocytes with micronuclei determined in samples of bone marrow. Positive controls were killed 24 hours after dosing.

Results:

DPX-Y6202 treated animals: Negative results.

Positive controls: positive

Comments:

(i) No clinical effects mentioned, hence, presumed "insufficient dosage."

(ii) Only one sampling time (6 hrs.) included for DPX-Y6202 treated animals. [If compound had effect of delaying maturation of treated progenator cells in marrow, an effect wouldn't be seen until release from delay (say at 24 hrs. after dosing, the time used in the mitomycin-C group)].

Evaluation:

Unacceptable.

TOXICOLOGY BRANCH
DATA REVIEW

004589

Study Type: Chromosome aberrations in CHO cells in vitro

Accession Number: 250071 (C 8)

MRID Number:

Sponsor: Du Pont

Contracting Lab: Nissan Chem. Ind. Ltd.

Date: Febuary 1983

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy] ethyl ester, (99.1%), DPX-Y6202, NC 302

Protocol:

Activity of chromosomal aberrations in Chinese hamster cell live with and without rat liver microsome fraction (S-9, from Arclor 1254 stimulated microsomes). Concentrations were from 125 to 1000 ug/ml for non-activation assay and 31.3 to 500 ng/ml for activation assay. Treatment times were 24 and 48 hours for non-activation and 24 hours for activation-assay. DMN was postive control substance.

Results:

"Treatment of the cells with NC302 at any concentration with or without S-9 Mix did not result in chromosomal aberrations. Cytotoxicity was observed in the cells treated with NC302 at 500 ug/ml in the presence of S-9 Mix." Results for positive control were positive.

Conclusions:

Negative for chromasome aberrations

Evaluation:

Acceptable

TOXICOLOGY BRANCH DATA REVIEW 004589

Study Type: Mutagenicity testing in microbial systems

Accession Number: 250071 (9)

MRID Number:

Sponsor: DuPont

Contracting Lab: Nissan Chem Ind., Ltd.

Date:

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-, ethyl ester (99.1%). DPX-Y6202, NC 302.

Protocol: Unknown

1. Recombinant assays (spot tests) were made using Bacillus subtillis M45 and H17 strains to assess DNA damaging capability. Concentrations were from 20 through 2000 ug/disk. Mitomycin-C was positive control substance.

2. Reversion assays in E. coli WP-2 and S. typhimurium TA1535, TA1537, TA1538, TA98, and TA100 strains (Ames tests) with and without S-9 activation were done. Concentrations were from 10 through 2500 ug/plate. Negative control was DMSO. The following positive controls were used.

WP2hcr- AF-2 (0.04 ug/plate)
TA1535 -propiolactone (5 ug/plate)
TA1537 9-aminoacridine (200 ug/plate)
TA1538 2-nitrofluorene (5 ug/plate)
TA98 AF02 (0.02 ug/plate)
TA100 AF-2 (0.01 ug/plate)

Results:

1. Recombinant assay tests were negative. Positive control was positive.

2. All reversion assay plate tests (including pre-incubation tests) were negative with and without S-9 activation.

Conclusions:

Neither DNA damaging capability or genetic activity were demonstrated in any of the in vitro assays conducted.

Evaluation:

Acceptable

TOXICOLOGY BRANCH DATA REVIEW

004589

01-10

Study Type: Teratology

Accession No.: 250071(C 10)

MRID No.:

Sponsor: DuPont

Contracting Lab: Nissan Experimental Medical Research Inst., Ltd.

Date: January, 10, 1983

Test Material: Ethyl 2-[4-(6-chloro-2-quinoxalyloxy)phenoxyl] propionate (99.1%), NC 302, DPX-Y6202.

Protocol: Pregnant rats were allocated at random to the following experimental groups.

Experimental groups	Substance Administered	Dosage	Amount of suspension containing dosage (mg/kg)	No. of cases	
				Laparotomized subgroup	Nursing subgroup
Control group	0.5% CMC	2mg/kg	2	21 dams	14 dams
Positive control group	Vitamin A	600000 IU/kg	2	20 dams	x
Small-dosage group	NC-302	30 mg/kg	2	21 dams	13 dams
Medium-dosage group	NC-302	100 mg/kg	2	22 dams	13 dams
Large-dosage group	NC-302	300 mg/kg	2	24 dams	14 dams

All doses were adjusted to 2 ml/kg with the solvent, 0.5% CMC.

Dosing was by gavage on days 6 through 15 of gestation.

Laparotomized subgroup was killed on day 21 The nursing subgroup was maintained three additional weeks. Four days after birth four young of each litter were selected at random to remain alive 8 weeks.

Results

There were no deaths, abortions or remarkable signs observed for DPY-Y6202 treated rats.

In rats given 300 mg/kg, gain in body weight was inhibited, food consumption decreased, and liver weight increased during the period of pregnancy. Gain in body weights was also inhibited in the 100 mg/kg group.

Also in the 300 group there was a statistical increase in occurrence of skeletal variation (mostly fourteenth rib variety).

The average number of corpora lutea per litter decreased in the 100 mg/kg group and the rate of implantation increased in the 100 and 300 mg/kg groups.

Body weights and food consumption of the young (F1) of the 300 mg/kg nursing group were decreased but no abnormality was found in frequency of 14th-rib variation.

No decrease in reproductive ability demonstrated.

No differences were found in the young (F1) using function, open field, or learning tests.

Conclusions:

No terata were seen in rats. Maternal NOEL: 30 mg/kg/day, 10 days (6-15 of gestation). Maternal LEL: 100

Core classification:

Minimum for teratology. Supplementary as a reproduction study.

004589

TOXICOLOGY BRANCH DATA REVIEW

Study Type: 90-Day Feeding Study in Rats

Accession No.: 250072

MRID No.:

Sponsor: DuPont

Contracting Lab: Nissan Chem. Ind. Ltd.

Date: January, 25, 1982

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxyl]-, ethyl ester

DPX-Y6202, NC302

Protocol: There were 4 treatment groups (including one untreated control), each consisting of 20 males and 20 females. The rats were randomly allocated by computer program to the 4 treatment groups as follows:

Group	Treatment level (NC-302 ppm)	Rat Nos. Male	Female
1	0 (Control)	1-15(16-20)	81-95 (96-100)
2	40	21-35(36-40)	101-110, 116-120(111-115)
3	128	41-55(56-60)	121-135(136-140)
4	1280	61-75(76-80)	141-155(156-160)

Rat Nos. in parentheses were maintained on a 6-week recovery phase following the termination of treatment.

Treatment diet was administered for 13 weeks, then 15 of the 20 rats per groups were killed and examined. 5% of each group were allowed a recovery period of 6 weeks before being killed.

Results:

Liver weight increases (compared to controls) were found in the 1280 ppm dosage group and to a lesser extent in the 128 level but not at the 40 ppm level. Microscopically seen were slight to minimal centrolobular and/or midzonal enlargement. These changes appeared to be reversible. During the recovery period the ratio of animals with liver lesions was reduced to 3 of 5 instead of 14 of 15 found at end of treatment.

Kidney weights were increased in females at the 1280 and 128 ppm levels but not at 40 ppm.

Testes decreased significantly in 13 of 15 males at the 1280 ppm level and to a lesser extent at the 128 level. Decreased testicular weight was still found after the recovery period ($P<0.01$ for high dosage).

Testicular atrophy and suppression of spermatozoa were also found after the recovery period in 3 of 5 males in the highest dosage group.

Decreases in pituitary weight for all treated females were considered "marginal" but were significant. No morphological changes were reported. Pituitary weight differences were dose-related at all levels including the 40 ppm level.

Conclusions:

A no-observed effect level was not demonstrated.

Pituitary effects in females were seen at all treatment levels. Testicular effects, including atrophy, persisted beyond the recovery period and may be accumulative.

Core classification:

Supplemental.

↑ Should be minimum data.

004589

TOXICOLOGY BRANCH DATA REVIEW

Study Type: Skin sensitization in guinea pigs

Accession Number: 250554

MRID Number:

Sponsor: DuPont, Haskell Lab No. HLO 182-83

Contracting Lab: Hazleton Labs Project No. 201-591

Date: 5/20/83

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxy]-ethyl ester. EC formulation (10.5%) DPX-Y6202-7

Protocol:

48 hours after 10 guinea pigs had been used for a dermal irritation study, they were sensitized by i.d. injection of 0.1 ml of DPX-Y6202-7 (the 10.5% formulation) in the back of each, once a week for 4 injections.

Thirteen days after the last injection 0.05 ml of undiluted test material and 0.05 ml of 10% test material in saline were applied to separate test sites on the backs of each sensitized guinea pig. Ten unsensitized control animals were challenged in the same way. Responses to challenge were compared.

Results:

One animal died after an injection.

Draize scores resulting from challenge are attached.

Conclusions:

The following inadequacies were found:

1. No positive control information was presented.
2. Sex of animals was not indicated.
3. Induction exposure appears to have been inadequate because:
   a. Induction dosage did not cause irritation in all animals although the test substance is irritating.
   b. Induction exposure was by i.d. injection, only once a week for 4 weeks.

004589

c. Results were considered negative by Haskell Lab., although scores resulting from challenge do show irritation in more animals of the sensitized group than of the unsensitized control group.

Core Classification: Supplemental

004589

Table 4

Individual Dermal Irritation Scores
Primary Irritation and Sensitization Study in Guinea Pigs
INY 6202-7 (14,809)
Challenge Phase
Test Animals

Animal Number	Site Number	Dose Level (%)	Observations			
			24 Hours		48 Hours	
			Erythema	Edema	Erythema	Edema
H04264	1	10	0	0	0	0
	2	100	1	0	1	0
H04265	1	10	0	0	0	0
	2	100	1	1	1	0
H04266	1	10	1	0	0	0
	2	100	1	1	1	0
H04267	1	10	0	0	0	0
	2	100	1	0	1	0
H04269	1	10	1	0	0	0
	2	100	1	1	1	0
H04270	1	10	0	0	0	0
	2	100	1	1	0	0
H04271	1	10	0	0	0	0
	2	100	1	0	0	0
H04272	1	10	0	0	0	0
	2	100	1	1	1	0
H04273	1	10	0	0	0	0
	2	100	1	0	0	0
			9/9	5/9	6/9	0/9

Table 4 - Continued

Individual Dermal Irritation Scores
Primary Irritation and Sensitization Study in Guinea Pigs
INY 6202-7 (14,809)
Challenge Phase
Control Animals

Animal Number	Site Number	Dose Level (%)	Observations			
			24 Hours		48 Hours	
			Erythema	Edema	Erythema	Edema
H04294	1	10	0	0	0	0
	2	100	1	1	0	0
H04295	1	10	0	0	0	0
	2	100	1	1	0	0
H04296	1	10	0	0	0	0
	2	100	1	0	0	0
H04297	1	10	0	0	0	0
	2	100	1	0	1	0
H04298	1	10	0	0	0	0
	2	100	1	0	0	0
H04299	1	10	0	0	0	0
	2	100	1	0	0	0
H04300	1	10	0	0	0	0
	2	100	1	0	1	0
H04301	1	10	0	0	0	0
	2	100	1	0	0	0
H4302	1	10	0	0	0	0
		100	1	0	1	0
H4303	1	10	0	0	0	0
	2	100	1	0	0	0
			10/10	2/10	3/10	0/10

DL-FW

TOXICOLOGY BRANCH DATA REVIEW

004589

Study Type: Six-months feeding study in dogs.

Accession No.: 250553, replacement for 250074

MRID No.:

Sponsor: DuPont

Contracting Lab: Nissan Chem. Ind. Ltd.

Date: April 28, 1983

Test Material: 2-[4-(6-Chloroquinoxalin-2-yloxy)-phenoxyl]-, ethyl ester (99.1%).

DPX-Y6202, NC302.

Protocol:

The following table indicates the design of this six-months feeding study in 5 months old dogs.

Group of administration	No. of Animals used		Animal No.	
	Male	Female	Male	Female
0 ppm	6	6	1101-1106	2101-2106
25 ppm	6	6	1201-1206	2201-2206
100 ppm	6	6	1301-1306	2301-2306
400 ppm	6	6	1401-1406	2401-2406
Total	24	24		

Results:

No dogs died during the feeding.

Interstitial pneumonia was present in every animal. Ovaries and uterus tended to decrease in absolute weight and in relative organ to body weights of females in the 100 ppm group. The same values increased at the 400 ppm level as shown in the following table.

Absolute	Control	25 ppm	100 ppm	400 ppm
uterus weights	8.50 ± 2.85	6.73 ± 2.46	2.67 ± 0.27	13.16 ± 3.93
Percent of body weights	0.06 ± 0.02	0.06 ± 0.02	0.03 ± 0.02	0.10 ± 0.03

The incidence of corpora lutea (shown below) correlates with uterus weights.

	0	25 ppm	100 ppm	400 ppm
Corpora lutea	5-1	0i	0	0i
	0i	4-0	0	2-2
	0i	2-4	5-6	5-3
	3-3	0	0	3-2
	0i	3-3	0	3-6
	2-2	0	0	2-4
Total	16	16	11	32

The incidence of corpora lutea is shown separately for each ovary.

i indicates immature ovaries and no corpora lutea.

Testicular atrophy was seen in 2 of 6 males in the 400 ppm group and testicular infection in another of the same group.

Conclusions:

NOEL 25ppm
LEL 100ppm

Core classification:

Guideline.

DCR-10638:W.ThomasEdwards:TOX-27:Rm824:CM-2:557-1511:7/29/83:efs

OL 13

004589

TOXICOLOGY BRANCH DATA REVIEW

Study Type: 90-Day Feeding Study in Mice

Accession No.: 250073

MRID No.:

Sponsor: DuPont

Contracting Lab: Nissan Chem. Ind. Ltd.

Data: June 24, 1982

Test Material: 2-[4-(6-chloroquinoxalin-2-yloxy)-phenoxyl]-, ethyl ester

DPX-Y6202, NC302

Protocol:

Dosages of mice were as follows:

Group	No. of Animals		Dietary Level
	Male	Female	ppm
1 (Control)	20	20	0
2 (Low-)	20	20	100
3 (Mid-)	20	20	316
4 (High-)	30	30	1000

All mice were killed after 13 weeks except that 10 males and 10 females of group 4 were fed normal rations for 4 more weeks, a recovery period.

Results:

There was no significant difference in survival between groups.

Swollen abdomens were observed during the dosing period but not after the recovery period.

Significant organ weight to body weight differences were seen in all treated mice. These included ratios for livers of males and females, adrenals in males in the mid and high-dose groups. Changes in testes were not dose related. Incidences of liver discoloration were seen in all treated groups and appeared to be dose related. Discoloration was reversible.

Compound-related lesions were observed in the liver of both sexes, adrenal gland of male mice, and ovaries of female mice. Liver changes were seen at all dose levels. The liver changes were diffuse hepatocytic hypertrophy/hyperplasia, degeneration/necrosis of individual hepatocytes, bile duct hyperplasia and green-brown pigment. The diffuse hepatocytic hypertrophy/hyperplasia was reversible in recovery animals while bile duct hyperplasia and green-brown pigment was still evident. Degeneration/necrosis of individual hepatocytes was observed in five of nine recovery male mice. Diffuse cortical cell hypertrophy was increased in incidence in the adrenal gland of high-dose male mice.

Increased numbers of corpora lutea appeared to be dose related (18/19 in high dosage level female group). At the end of the recovery period 6/9 females still had increased numbers of corpora lutea but change was less severe.

Conclusions:

Liver changes were seen at all dosage levels. Increased corpora lutea appeared to be dose related and some excess persisted through the recovery period.

A no-observed-effect level was not determined.

Core classification:

Supplemental

Should be minimum dl